REMARKS

I. Status of the Application

Claims 1, 2, 4-9, 14, 20, 21 and 24 are presently pending in the application. Claims 1, 2, 4-9, 14, 20, 21 and 24 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Claim 14 stands rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement. Claim 24 is rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. Claim 14 is rejected under 35 U.S.C. § 112, first paragraph, as containing new matter. Claim 5 is objected to as being of improper dependent form.

Applicants have amended the claims under consideration to more clearly define and distinctly characterize Applicants' novel invention. Claim 24 was amended to recite an "isolated" host cell, support for which can be found at least at paragraph [0023] of the published application, where Applicants teach a host cell comprising a nucleic acid according to the invention, and at paragraph [0043] of the published application, where Applicants teach isolated cells. The specification was amended to include a Brief Description of the Drawings section. Support for this amendment can be found at least at paragraphs [0072] – [0077] of the published application and at the sequence listing.

Applicants respectfully submit that the amendments presented herein contain no new matter and do not raise new issues requiring further search. Applicants respectfully request entry and consideration of the foregoing amendments, which are intended to place the case in condition for allowance.

II. Objections

The specification is objected to because, the Office Action asserts, Figure 1 has no sequence identifier and no brief description of the drawing. In response, Applicants have amended the specification to include a Brief Description of the Drawings section. This section recites a description of Figure 1 that includes a sequence identifier, i.e., SEQ ID NO:5. Accordingly, Applicants respectfully request that the objection to the specification be reconsidered and withdrawn.

Claim 5 is objected to under 37 C.F.R. § 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. The Office Action states that Applicants are required to cancel the claim, or amend the claim to place the claim in proper dependent form, or to rewrite the claim in independent form. The Office Action asserts that claim 1 already recites a nucleic acid of interest and, accordingly, claim 5 fails to limit claim 1. Applicants respectfully traverse this objection.

Applicants disagree with the Office Action's assertion that claim 1 "already recites a nucleic acid of interest." Claim 1 recites that the nucleic acid sequence "allows expression of a nucleic acid sequence of interest operably linked to said promoter in a cancer cell in an epithelium-selective manner." Accordingly, the nucleic acid sequence recited in this claim is ***capable*** of expressing a nucleic acid sequence of interest, but ***does not require*** that a nucleic acid sequence of interest be present in the claimed isolated or recombinant nucleic acid sequence. In contrast, claim 5 requires the claimed isolated or recombinant nucleic acid sequence to include the presence of a nucleic acid sequence of interest. Thus claim 5 further limits the subject matter of claim 1. Accordingly, Applicants respectfully request that the objection of claim 5 be reconsidered and withdrawn.

III. The Specification Provides Adequate Written Description for the Pending Claims

At page 3 of the instant Office Action, claims 1, 2, 4-9, 14, 20, 21 and 24 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse this rejection. Applicants respectfully submit that the specification provides adequate written of the claimed nucleic acid sequence, and that one of skill in the art would readily understand the structure of the claimed nucleic acid sequence based on Applicants' teachings.

The Office Action asserts, "the mere presence of said binding sites within the claimed sequence does not indicate that the claimed sequence can direct epithelial specific transcription. Contrary to Applicant's assertion, the mere presence of putative binding site of Ets and Sp-1 does not necessarily result in epithelial specific expression," that "[t]he specification does not teach whether the claimed region of 365 bp confer epithelial specific expression although Ets and Sp1 binding sites are presented in this region," and that "[t]he mere presence of Ets and Sp1 putative binding site within the claimed nucleic acid sequence is not sufficient structurally for the claimed function" (paragraph bridging pages 4 and 6). Applicants disagree with these assertions.

First of all, Applicants are not claiming the "mere presence" of Sp-1 and Ets sites. Instead, Applicants are claiming a ***specific nucleic acid sequence*** having Ets binding sites and an Sp-1 binding site at ***specific positions*** of the claimed sequence, i.e., a promoter region encoding nucleotides ***3200 to 3556 of SEQ ID NO:5*** or a nucleic acid sequence functionally equivalent thereto, and comprising ***Ets binding sites*** at about nucleotides ***3223, 3451 and 3520 of SEQ ID NO:5*** and an ***Sp-1 binding site*** at about nucleotide ***3274 of SEQ ID NO:5***. Thus, the claimed binding sites have a ***specific spatial distribution within the claimed promoter region sequence.*** The claimed promoter region having a specific spatial distribution of Ets and Sp-1 binding sites provides a ***structural feature*** that correlates with the claimed ***function*** of allowing ***expression*** of

a nucleic acid of interest operably linked to the promoter in a cancer cell ***in an epithelium-selective manner***.

Applicants have experimentally demonstrated that the claimed promoter region containing the specific spatial distribution of binding sites claimed by Applicants ***confers epithelial-specific expression*** of an operably linked nucleic acid sequence of interest. Although the instant Office Action asserts that the specification does not teach whether the claimed region of 365 bp confer epithelial specific expression although Ets and Sp-1 binding sites are presented in this region, this is simply not the case. The Examiner's attention is respectfully directed to paragraph [0076] and Figure 2 of the published application. Here, Applicants describe the results obtained using different promoter deletion eGFP fusion constructs. Expression of the eGFP reporter was investigated in non-epithelial cells (FLF and HUVEC) and epithelial cells (SW948 and COS-7). Applicants discovered that a construct containing the first 146 base pairs of the promoter region ($p39^{E12-3}$) had ***no promoter activity*** in any of the four cell types. A construct containing the first 442 base pairs of the promoter region ($p39^{E11-1}$) promoted eGFP ***expression in both non-epithelial and epithelial cells***. Thus, although the first 442 base pairs could promote gene expression, such expression was ***not epithelial cell-specific***. Applicants then determined that a construct containing the first 778 base pairs of the promoter region ($p39^{E4-1}$) or larger clearly demonstrated ***epithelial-specific expression***. eGFP was detected only in the epithelial SW948 and COS-7 cells, and not in the non-epithelial FLF and HUVEC cells. One of skill in the art would readily understand this experiment to evidence that the minimal essential promoter region generating epithelial specificity is found in the promoter fragment between base pair 442 and base pair 778. Thus, Applicants have experimentally demonstrated that this 336 base pair region of the promoter sequence does in fact result in ***epithelial-specific expression***.

For at least these reasons, the instant specification provides adequate written description

for the claimed invention. Accordingly, the Examiner is respectfully requested to reconsider and withdraw this rejection of claims 1, 2, 4-9, 14, 20, 21 and 24 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

IV. Claim 14 Is Enabled

At page 6 of the instant Office Action, claim 14 stands rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The Office Action states that the instant specification does not provide any *in vitro* or *in vivo* data that demonstrates the medicament as claimed is effective in treating epithelial cancer. The Office Action concludes that, for the reasons set forth in the instant and previous Office Actions, the claimed medicament is not enabled. Applicants respectfully traverse this rejection.

Claim 14 is directed to a medicament for treating ***epithelial cancer*** comprising an isolated or recombinant nucleic acid sequence comprising a promoter region encoding nucleotides 3200 to 3556 of SEQ ID NO:5 or a nucleic acid sequence functionally equivalent thereto, and comprising Ets binding sites at about nucleotides 3223, 3451 and 3520 of SEQ ID NO:5 and an Sp-1 binding site at about nucleotide 3274 of SEQ ID NO:5, wherein said nucleic acid sequence allows expression of a nucleic acid sequence of interest operably linked to said promoter in a cancer cell in an epithelium-selective manner, wherein said nucleic acid sequence of interest is a ***suicide gene***. Applicants respectfully submit that the instant specification provides ample direction and guidance to make and use the claimed medicament.

Applicants provide an animal model that ***phenotypically correlates to epithelial cancer*** (See paragraphs [0070] to [0071] of the published application). The instant specification teaches an *in vivo* EGP-2 transgenic mouse epithelial tumor model that expresses the human EGP-2 protein accurately and has been demonstrated to exhibit a similar distribution pattern to that

observed in humans (paragraph [0071] of the published application). Applicants' transgenic mouse tumor model displays the immunological tolerance frequently observed in cancer patients against tumor antigens, which is of great significance since the mechanisms that regulate immunological tolerance to tumor antigens are formidable obstacles that withstand effective tumor immunotherapy in cancer patients. *Id.* Further, Applicants teach that EGP-2 is one of the best-studied tumor-associated antigens frequently used as an attractive target for experimental and clinical cancer therapy (paragraphs [0070] and [0068] of the instant specification).

Applicants reiterate that the instant specification and the state of the art at the time of filing the instant application reflect the fact that suicide genes and their prodrugs were well known (*See* section V of Applicants' Amendment and Response filed September 5, 2006). Applicants also reiterate that the instant specification teaches the nucleic acid sequence of SEQ ID NO:5, the sequences of Ets and Sp-1 binding sites, that these binding sites could modulate epithelial-specific gene expression, and that sequences of many such binding sites were known in the art at the time of filing.

Based on Applicants' teaching of a working transgenic mouse model of epithelial cancer, Applicants' teaching of the claimed isolated or recombinant nucleic acid sequence, and the knowledge in the art of suicide genes, Applicants' specification, coupled with the level of skill in the art, readily enables a person of skill in the art to make and/or use the claimed invention. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of claim 14 under 35 U.S.C. § 112, first paragraph, as lacking enablement.

V. Claim 24 Is Directed to Statutory Subject Matter

At page 8 of the instant Office Action, claim 24 stands rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. The instant Office Action asserts that the term "host," as defined by the specification at page 9, lines 27-29, states that the cell is present or intended to be present in a human being, said cell becoming integrated into the human being and, therefore, being an inseparable part of the human itself. The Office Action concludes that the scope of the claim encompasses a human being which is non-statutory subject matter. The Office Action suggests that recitation of the limitation "an isolated" or "in vitro" would be remedial.

Without acquiescing to the rejection, Applicants respectfully submit that claim 24 has been amended to recite "an isolated" host cell, as helpfully suggested by the Examiner. Accordingly, Applicants respectfully request that the rejection of claim 24 under 35 U.S.C. § 101 as being directed to non-statutory subject matter be reconsidered and withdrawn.

VI. Claim 14 Is Not Directed to New Matter

At page 8 of the instant Office Action, claim 14 stands rejected under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. The Office Action asserts that the claim contains subject matter which was not described in the specification in such a way as to reasonable convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Office Action asserts that the instant specification discloses that the medicament is for treatment of cancer or preferably carcinoma, not for epithelial cancer. The Office Action concludes that the newly introduced limitation of treating epithelial cancer constitutes. Applicants respectfully traverse this rejection.

Applicants' specification provides support for epithelial cancer. Applicants respectfully

direct the Examiner's attention to the bottom of paragraph [0013] of the published application, where Applicants teach, "Expression of a nucleic acid of interest operably linked to a promoter or a functional fragment thereof as provided by the invention is thus mainly restricted to normal adult non-squamous epithelium or neoplasias ***derived from epithelia***..." (emphasis added). The instant specification further teaches, that ***carcinomas*** "in general are the malignant counterparts or neoplasia ***derived from epithelia***" (paragraph [0002] of the published application, emphasis added).

Thus, the instant specification provides support for epithelial cancer. Accordingly, Applicants respectfully request that the rejection of claim 14 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement be reconsidered and withdrawn.

VI. CONCLUSION

Having addressed all outstanding issues, Applicants respectfully request reconsideration and allowance of the case. To the extent the Examiner believes that it would facilitate allowance of the case, the Examiner is requested to telephone Applicants' attorney at the number below.

Respectfully submitted,

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